This is a smattering of information on quite a large topic. You can't possibly know everything about breast cancer, but here are the highlights.

Pathology

There are a few ways someone can end up with breast cancer. The first is through **estrogen**. The more estrogen a woman is exposed to the greater her chances of breast cancer. This means that **early menarche**, **late menopause**, **nulliparity** and **hormone replacement therapy** (OCPs don't count) increase her risk. The second is to get **radiation** to the chest (like from treatment of Hodgkin's Lymphoma). The third is genetics - mainly the **BRCA1/2** mutation that substantially increases the risk of "lady cancers" (Breast and Ovarian).

Patient presentation

There are three main presentations. The first is the **asymptomatic screen** (the way we should find breast cancer). The second is the **breast lump,** which requires us to determine whether it's cancer or not. The third is **obvious cancer** with the skin dimpling, fixed, firm axillary nodes, and an obvious large, fixed breast mass. Regardless of how the diagnosis is arrived at, the therapy will depend on the stage and the biopsy.

Screening

Mammogram is the screening test of choice. There's a bit of a controversy around when to start. The USPSTF recommends starting at 50 years old and screening every two years (**50q2y**) while the ACS/NCI says to start at 40 and screen annually (**40q1y**). 40q1y catches more cancer but puts a larger number of women through unnecessary testing and more complications. 50q2y is an attempt at balancing risk and benefit; curing cancer vs avoiding unnecessary procedures and cost-conscious care. There isn't a right answer.

Other options exist, however. The **MRI** is the **best screen** but is cost prohibitive. MRI should be chosen as a screening (rather than diagnostic) tool in patients with extremely high risk. That is, people with a super strong family history or those who have received radiation.

Self-exams and **clinical exams** do **NOT BENEFIT** anyone. Don't do them. Just screen with mammograms and MRI.

ETIOLOGY →	PRECANCER →	CANCER
ESTROGEN - Obesity - Nulliparity - Early Menarche - Late Menopause - HRT **GENES** - BRCA 1/2 - Radiation	"pre-cancer" is Carcinoma in Situ For breast cancer	Adenocarcinoma
Identify and Modify Risk Factors	Local Resection is curative	Surgery, Radiation and/or Chemo
	Screen if able	Diagnose and stage
Prophylactic Mastectomy (BRCA1/2 only)	Mammogram MRI (High risk)	Core Needle Biopsy SLNB --> ALND

Conflicting Recommendations

USPTF: Start at 50, screen every 2 years, **50q2y**
ACS/NCI: Start at 40, screen every 1 year, **40q1y**

Picking the test

If you screen: Mammogram first
If you diagnose: Mammogram first
If high risk (BRCA or Radiation): MRI
If young (see next page): Ultrasound

Diagnosis

This is actually quite a complex concept – what do you do for a woman with a breast mass? Let's start with what's certain.

Biopsy is the answer. If there's a chance it's cancer, we want to do a biopsy. But which? A **fine needle aspiration** is sufficient when there's a cyst and the thought is it's NOT cancer (see <30 years old). An **excisional biopsy** is the choice when it's so obvious it's cancer - just take it out. The standard, and what should be associated with the diagnosis of breast cancer, is the **core-needle biopsy.** It takes a large piece of tissue and allows for lots of stains (bigger than an FNA) but is breast conserving (isn't an excision).

Patient screens positive on mammogram? Biopsy. High suspicion it's cancer? Biopsy. But - when a woman is young (<30 years old) the likelihood of something else is so high that thoughts shouldn't jump to a biopsy. In a young woman start with **reassurance** (watch and wait to see if a lump goes away). If that doesn't work, pick an **ultrasound**. If the ultrasound shows a cyst, **aspirate** it. If it goes away or shows an infection, done. But, if the ultrasound shows a mass, the aspirate blood, the mass comes back, or she's older than 30 years old go to a diagnostic mammogram and biopsy.

Treatment

The treatment is based on the **stage**. Staging isn't required for a medical student, but it's included to the right just in case. See the next page, right column, to tie together stage with treatment.

There are multiple elements to treatment in breast cancer:

Surgery. A lumpectomy + axillary lymph node dissection (ALND) + radiotherapy (RT) is equal to a mastectomy + axillary lymph node dissection (ALND) for local control. A sentinel lymph node dissection should be made prior to ALND in order to avoid the morbidity associated with lymphedema. If a sentinel node is negative, there's only a 5% chance that other nodes are involved.

Diagnostic Dilemmas

A lump, a lump! If < 30, start here, go 1-4		
	1.	< 30 = Reassurance (2-3 cycles)
Then	2.	<30 + persists = get ultrasound
Then	3.	<30 + ultrasound with cyst = aspirate
Then	4.	< 30 + cyst resolves = reassurance

But if at any time….

	1.	>30
OR	2.	Ultrasound shows mass
OR	3.	Aspirate is bloody
OR	4.	Cyst recurs

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Mammogram (diagnostic) → Biopsy

Simplified Staging of Breast Cancer (do not memorize)

STAGE	SIZE		NODES
Stage I	<2 cm	&	0
Stage II	<2 cm	&	1-3
		OR	
	2 - 5 cm	&	0-3
Stage III	-		+4
	>5cm		-
	Affixed to chest wall		
Stage IV	Distant Metastasis		

See it as…

Small = Stage I	No Nodes: Stage I
Middle = Stage II	Some Nodes: Stage II
HUGE = Stage III	LOTS of Nodes: Stage III

Chemo. Chemo is often anthracycline-based (Doxorubicin-Cyclophosphamide) with a taxane (Paclitaxel). It can be neoadjuvant (before surgery) or after surgery (adjuvant). Know that Doxorubicin causes a **dose-dependent irreversible CHF**.

Targeted Therapy. Part of the biopsy is to determine if the lesions have tumor markers.

Her2Neu is a tyrosine kinase associated with worse prognosis, but also provides a targeted chemotherapeutic agent. **Trastuzumab** inhibits Her2Neu. It causes a **dose-independent reversible CHF**, and therefore q3month Echocardiograms are required for patients receiving this medication.

Estrogen (ER) and Progesterone (PR) receptors allow for endocrine therapy. Which therapy the patient gets is dependent on menopause. For **premenopausal** women, use **Selective Estrogen Receptor Modulators (SERMs)** such as **tamoxifen** (stronger, causes DVT, causes endometrial cancer) or **raloxifene** (weaker, no DVT, no endometrial cancer). For **postmenopausal** women, use **aromatase inhibitors** like anastrozole.

Prevention

Trastuzumab and **Doxorubicin** cause heart failure. Get Echocardiograms throughout treatment.

SERMs have been shown to reduce the incidence of invasive breast cancer in women who are post-menopausal and have increased lifetime risk for Breast Ca.

BRCA1/2 gets prophylactic mastectomy and bilateral salpingo-oophorectomy. If she really doesn't want that, annual MRI and mammography is indicated.

Keep in mind this is trying to SUPER simplify things

Carcinoma In Situ: Breast Conserving Therapy
- Lumpectomy + RT + ALND
- Mastectomy + ALND

Invasive Carcinoma – Systemic therapy
- Mastectomy + ALND + Chemo + Targeted
- Lump + RT + ALND + Chemo + Targeted

Neoadjuvant chemo (before surgery)
- Inflammatory breast cancer
- Locally Advanced (Stage IIIa)

Adjuvant Chemo (after surgery)
- Stage I and II

Local Control:
- Surgery
- Radiation

Systemic therapy
- Chemotherapy
- Targeted therapy

Treatment based on biopsy and stage

Her2Neu +	Trastuzumab
Her2Neu -	No option
ER/PR + & postmenopause	Aromatase-Inhibitors
ER/PR + & premenopause	SERM
ER/PR -	No option
Stage 1 - 4	CHEMO - Anthracycline - Cyclophosphamide - Paclitaxel

High Yield Associations for Breast Ca Treatment

Tamoxifen	Better, ↑DVT, ↑ Endo Ca
Raloxifene	Worse, ↓DVT, ↓ Endo Ca
Trastuzumab	Heart Failure, Reversible, EARLY
Doxorubicin	Heart Failure, Irreversible, LATE
Daunorubicin	The other Doxorubicin
BRCA 1/2	Ppx Bilateral Mastectomy + BSO
ALND	Sentinel Lymph Node First